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Gene interaction network analysis in Wolf-Hirschhorn Syndrome

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Introduction and objectives: Deletions in the 4p16.3 region cause Wolf-Hirschhorn syndrome (WHS), a contiguous gene deletion syndrome involving variable size deletions. This study aimed to perform a gene interaction network analysis within the WHS critical region and to stablish the cytogenomic profile of the chromosome rearrangements involving the 4p16.3 region. Material and methods: 16 samples from individuals with a clinical indication of WHS were retrospectively analyzed of which 9 had a cytogenetic visible deletion and 7 a submicroscopic deletion not previously identified. Using FISH, chromosomal microarray analysis and whole exome sequencing, we define the critical breakpoints within the 4p16.3 chromosome rearrangements. Gene Multiple Association Network Integration Algorithm (GeneMANIA) version 3.1.2.8, available at http://www.genemania.org/ was used to identify protein–protein interactions (PPI). In the present study, the association data of GeneMANIA was based on the PPI databases and co-expression profiles, in which each interaction between proteins are experimentally proven. Results and conclusion: In addition to 12 classical terminal deletions, we mapped 1 interstitial deletion, 2 ring chromosomes and 1 typical translocation 4;8. The deletions sizes ranged between 3.7 and 26 Mb. We fully characterized the 4p deletions in 8 samples. An initial genes list from 343 genes a interactome network composed by 136 nodes and 750 edges was obtained. From these nodes, GO categories were identified as more significant as positive regulation of vasoconstriction and dopamine receptor signaling pathway. 4p chromosomal rearrangements associated with WHS have different mechanisms of origin, which leads to a heterogeneous spectrum of phenotype features, from very subtle or mild, to a wide range of severe abnormalities. The critical region in our study includes four candidate genes (TACC3, FGFR3, LETM1, and WHSC1) associated with seizures and microcephaly. Spaning a common region of 170 kb. This study refined the critical chromosomal susceptibility region within 4p16.3 and is further exploring the gene interaction between candidate genes related to seizures and microcephaly associated with WHS. Keywords: microarray chromosome analysis, 4P16.3 Chromosome Rearrangements, gene interaction network